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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/003,400	10/22/2001	Neal D. Epstein	4239-61090	5338

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EXAMINER

LI, QIAN JANICE

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 02/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/003,400

Applicant(s)

EPSTEIN ET AL.

Examiner

Q. Janice Li

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10/30/04.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5,7-12,25,43,49 and 50 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5,7-12,25,43,49 and 50 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 October 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

The amendment and response filed 10/30/04 have been entered. Claims 1, 11, 25, 43, 49, and 50 have been amended. Claims 6 and 44-48 have been canceled. Claims 1-5, 7-12, 25, 43, 49, and 50 are pending and under current examination.

Previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated. Upon further review, new grounds of rejections are necessitated and appear below.

Claim Objections

Claim 12 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Specifically, in light of the teaching of the specification, the cell markers recited in claim 12 are necessarily present in all cardiomyocytes recited in claim 8 from which claim 12 depends from, thus claim 12 does not further limit the subject matter of claim 8.

Claim 25 is objected to because the phrase "less that" in line 4 should be "less than", and the phrase "suspension in the tissue culture medium" in line 10 should be "a suspension of the tissue culture medium".

Claim Rejections - 35 USC § 112

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 7-12, 25, 43, 49, and 50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The methodology for determining adequacy of Written Description to convey that applicant was in possession of the claimed invention includes determining whether the application describes an actual reduction to practice, determining whether the invention is complete as evidenced by drawings or determining whether the invention has been set forth in terms of distinguishing identifying characteristics as evidenced by other descriptions of the invention that are sufficiently detailed to show that applicant was in possession of the claimed invention (*Guidelines for Examination of Patent Applications under 35 U.S.C. § 112, p 1 "Written Description" Requirement*; Federal Register/ Vol 66. No. 4, Friday, January 5, 2001; II Methodology for Determining Adequacy of Written Description (3.)).

Claims 1-5, 7-12, 25, 43, 49, and 50 are drawn to a genus of mammalian cardiomyocyte precursor cells of skeletal muscle origin, which is isolated according to its size and surface marker c-kit and c-met. Given the broadest reasonable interpretation, the claims encompass cells isolated from any one of the mammalian species, and at any developmental stage, e.g. embryo, infant, or adult.

The specification teaches using the size and marker criteria for isolating cardiomyocyte precursor cells from *adult mice*, and evidenced the differentiation of the cells into beating cardiomyocytes. The specification goes on to teach using such standard for isolating cardiomyocyte precursor cells from adult human subject, however, the specification fails to teach that the isolated *human* cell population could differentiate into beating cardiomyocytes, and whether the skeletal muscle cells obtained from the embryo and infant mice or from any other species isolated according to such standard would be capable of differentiating into beating cardiomyocytes. The specification or post-filing publications (*Gopal et al*, 2001 &2002) provide only one species for the genus of the cardiomyocyte precursor cells derived from skeletal muscles, i.e. adult mice, and the post-filing publications call for further investigation concerning the existence of analogous cells in humans. In view of such, the disclosure fails to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention as they are broadly claimed.

In view of the state of the art and levels of the skilled in the art, it is well known in the art that cellular markers, particularly the stem cell markers such as c-kit and proto-oncogene markers such as c-met differentially expressed at various stages of the development. It is also well known in the art that there are about 4260 species of mammals known on the planet, wherein the mammals are as large as an elephant, and as small as a mouse, consequently the sizes of the skeletal muscle cells would be varied among the different species. Therefore, it is pivotal that the specification provides information on the marker distribution at different stages of the development and the

size difference for at least representative species of the genus. However, the specification is silent with respect to the species variations and marker dynamics essential for practice the invention, and therefore, it fails to provide an adequate written description commensurate with the scope of the claims.

The Revised Interim Guidelines state "THE CLAIMED INVENTION AS A WHOLE MAY NOT BE ADEQUATELY DESCRIBED IF THE CLAIMS REQUIRE AN ESSENTIAL OR CRITICAL ELEMENT WHICH IS NOT ADEQUATELY DESCRIBED IN THE SPECIFICATION AND WHICH IS NOT CONVENTIONAL IN THE ART" (Column 3, page 71434), "WHEN THERE IS SUBSTANTIAL VARIATION WITHIN THE GENUS, ONE MUST DESCRIBE A SUFFICIENT VARIETY OF SPECIES TO REFLECT THE VARIATION WITHIN THE GENUS", "IN AN UNPREDICTABLE ART, ADEQUATE WRITTEN DESCRIPTION OF A GENUS WHICH EMBRACES WIDELY VARIANT SPECIES CANNOT BE ACHIEVED BY DISCLOSING ONLY ONE SPECIES WITHIN THE GENUS" (Column 2, page 71436). The court has stated, "IN CHEMICAL CASE WHERE APPLICANT DISCLOSES THAT ONE SPECIES OF A CLASS OF CHEMICALS WILL ACCOMPLISH CERTAIN PURPOSE WITHOUT NAMING ANY OTHERS OF CLASS TO WHICH IT BELONGS OR WITHOUT SO DESCRIBING THE SPECIES AND ITS MODE OF OPERATION AS TO CALL ATTENTION TO FACT THAT OTHER MEMBERS OF CLASS ARE ITS EQUIVALENTS AND WILL PERFORM SAME FUNCTIONS, HE IS NOT ENTITLED TO BROADER SCOPE OF DISCLOSED INVENTION BY CLAIMING WHOLE GROUP EVEN THOUGH THOSE SKILLED IN ART MAY KNOW THAT IN SOME RESPECTS AT LEAST DIFFERENT MEMBERS OF GROUP ARE EQUIVALENTS; CERTAIN MEMBERS OF WELL-DEFINED GROUP OF CHEMICALS MAY BE EQUIVALENTS FOR ONE PURPOSE AND NOT EQUIVALENT FOR ANOTHER. ((*In re Soll*, 97 F.2d623, 38 USPQ 189 (CCPA 1938), emphasis added)).

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "APPLICANT MUST CONVEY WITH REASONABLE CLARITY TO THOSE SKILLED IN THE ART THAT, AS OF THE FILING DATE

SOUGHT, HE OR SHE WAS IN POSSESSION OF *THE INVENTION*. THE INVENTION IS, FOR PURPOSES OF THE 'WRITTEN DESCRIPTION' INQUIRY, *WHATEVER IS NOW CLAIMED*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for the characteristics of the genus of the mammalian cardiomyocyte precursor cells. Therefore, only the described adult mice skeletal cells meets the written description provision of 35 U.S.C. §112, first paragraph.

Claims 1-5, 7-12, 25, 43, 49, and 50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether the disclosure satisfies the enablement requirements and whether undue experimentation would be required to make and use the claimed invention (see *In re Wands*, 858 F. 2d

731, 737, 8 USPQ 2d 1400, 1404, 1988). These factors include but are not limited to the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, the breadth of the claims, and amount of direction provided.

As indicated *supra* in the written description section, the specification fails to provide an adequate description for the genus of the precursor cells of cardiomyocytes derived from skeletal muscle cells because the disclosure fails to describe the common attributes or characteristics that identify members of the claimed genus, cells from the adult mice skeletal muscle alone is insufficient to describe the genus, because it is unpredictable whether similar cells from a different species would fall into the bounds of criteria set forth in the claims.

In conclusion, one cannot extrapolate the teachings of the specification to the scope of the claims because the skilled artisan cannot envision the detailed characteristics that would reasonably cover the genus of cardiomyocyte precursor derived from skeletal muscle cells encompassed by these claims, thus would not know how to use the invention without first carrying out undue experimentation to determine whether the criteria set forth in the claims are universal for the genus of mammalian cardiomyocyte precursor cells.

Accordingly, in view of the limited guidance, the lack of predictability of the art, and the breadth of the claims, one skill in the art could not practice the invention without undue experimentation as it is broadly claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 25 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 25 is vague and indefinite because of the claim recitation, "a suspension of cells" in line 5, wherein the cells could refer to skeletal muscle cells, cardiomyocytes, or precursor cells. It is unclear which cells the claim refers to, and thus the metes and bounds of the claims are uncertain.

Claim 25 is vague and indefinite also because of the claim recitation, "the skeletal muscle cells" in line 6, wherein the cells could refer to the original population of skeletal muscle cells, or the population of skeletal muscle cells that are less than 40 μm in diameter. It is unclear which cells the claim refers to, and thus the metes and bounds of the claims are uncertain.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Amy Nelson** can be reached on 571-272-0804. The fax numbers for the organization where this application or proceeding is assigned are **703-872-9306**.

Any inquiry of formal matters can be directed to the patent analyst, **Dianiece Jacobs**, whose telephone number is (571) 272-0532.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is **703-308-0196**.

JANICE LI
PATENT EXAMINER



Q. Janice Li
Patent Examiner
Art Unit 1632

QL

February 2, 2004